

REMARKS

Priority

It is alleged that Applicant failed to provide an English translation of the Korean application No. 10-2003-0004521 and the priority date of the application is interpreted as January 19, 2004. Page 3 of the Office Action. Applicant submits herewith the English translation of the Korean application which shows the priority date of Jan 23, 2003, as the Examiner requested.

Claim 1 is Not Obvious over Kikuchi

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kikuchi *et al.* (US 2004/0022848, "Kikuchi"). (Pages 3-4 of the Office Action). In particular, it is alleged that Kikuchi *et al.* teach a pharmaceutical preparation obtained by primary granulation of a drug and a hydrophobic additive (waxy substance) (paragraphs 0061 and 0062), followed by secondary granulation of the obtained granules by wet granulation using a hydrophobic wet granulation material (see paragraph 0065). Page 3 of the Office Action. Applicant respectfully traverses the rejection.

Under the current law, prior art references cannot render a claim obvious unless the PTO provides evidence that the references meet a three-part test for *prima facie* obviousness. To begin with, the prior art reference or references must provide "motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant." See *In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000); *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d 1051, 1054 (Fed. Cir. 2005). Where one reference is relied upon by the PTO, there must be a suggestion or motivation to modify the teachings of that reference. See *In re Kotzab*, 217 F.3d at 1370, 55 U.S.P.Q.2d at 1316-17. Where an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. See *WMS Gaming Inc. v. International Game Technology*, 184 F.3d 1339, 1355, 51 U.S.P.Q.2d 1385, 1397 (Fed. Cir. 1999); *Princeton Biochemicals, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d at 1054; *Teleflex, Inc. v. Ficosa North America Corp.*, 299 F.3d 1313, 1334, 63 U.S.P.Q.2d 1374, 1387 (Fed. Cir. 2002).

Second, the prior art references cited by the PTO must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. See *In re Dow Chemical*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988); *Boehringer Ingelheim Vetmedica, Inc.*, 320 F.3d 1339, 1354, 65 U.S.P.Q.2d 1961, 1971 (Fed. Cir. 2003); *Noelle v. Lederman*, 355 F.3d 1343, 1352, 69 U.S.P.Q.2d 1508, 1516 (Fed. Cir. 2004). Further, "[b]oth the suggestion and the reasonable expectation of success 'must be founded in the prior art, not in the applicant's disclosure.'" *Noelle*, 355 F.3d at 1352, 69 U.S.P.Q.2d at

1515-16 (quoting *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991)). Finally, the PTO must show that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. See *Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1473, 43 U.S.P.Q.2d 1481, 1490 (Fed. Cir. 1997); *Litton Systems, Inc. v. Honeywell, Inc.*, 87 F.3d 1559, 1569, 39 U.S.P.Q.2d 1321, 1327 (Fed. Cir. 1996).

Claim 1 recites sustained-release preparations, which are prepared from double granules obtained by primary granulation of drug according to melt granulation using hydrophobic release-delaying additives, and then by secondary granulation of the obtained granules according to wet granulation using hydrophobic wet-granulation material.

On the contrary, the compositions of Kikuchi are prepared by spray granulation method using synthetic aluminium silicate and/or hydrous silicon dioxide (Kikuchi, paragraph [0004]). Although Kikuchi mentions a secondary granulation, it does not use hydrophobic materials, but hydrophilic materials such as erythritol and D-sorbitol. See, paragraph [0065] and [0085]. Kikuchi further discloses that a secondary granulation may be accomplished by melting granulation [paragraph 0065].

Thus, Kikuchi, which uses melting granulation and hydrophilic materials, does not disclose or suggest the preparation of instant claim 1 reciting wet granulation and hydrophobic materials. Kikuchi is missing teaching or suggestion of essential elements of the claimed invention. Kikuchi fails to suggest or motivate the preparations obtained by the wet granulation using hydrophobic material as recited in claim 1.

Because the preparations of instant claim 1 require wet granulation using hydrophobic materials as a secondary granulation, the present invention (1) minimizes the amount of hydrophobic additives, (2) imparts sustained-releasing property, (3) eliminates adhesion of granules occurring during tablet preparation, and (4) allows the production of a tablet easy and convenient (paragraph [0009]).

On the contrary, by the melting granulation disclosed in Kikuchi, the sustained-release preparations of the present invention cannot be achieved. As shown in Experimental example 1 of the present application, the preparation of Comparative example 1 has only the surface formed by melting granulation as in Kikuchi, and it exhibits serious adhesion in spite of addition of excessive amount of lubricant, making the tablet preparation impossible (paragraph [0032] of the present publication).

Therefore, Kikuchi, which uses melting granulation as a secondary granulation, teaches away from the sustained-release preparations of the present invention. Thus, Kikuchi does not provide one skilled in the art with any suggestion or motivation for the claimed sustained-release preparations.

Further, Kikuchi uses synthetic aluminium silicate and hydrous silicon dioxide to prevent adhesion of the granulated product onto the inside of a spray granulation apparatus (Kikuchi, paragraph [0004]). Thus, the technical solution used in Kikuchi is “to add synthetic aluminium silicate and hydrous silicon dioxide,” but not “secondary granulation” as in the present invention. In contrast to Kikuchi, the present invention minimizes the amount of hydrophobic additives for imparting sustained-releasing property (paragraph [0009]). Thus, Kikuchi does not provide to one skilled in the art any suggestion or motivation to select secondary granulation as recited in present claim 1.

In addition, Kikuchi does not teach or suggest the sustained-release preparation of the present invention. Example 2 of Kikuchi describes that the formed granules exhibited excellent drug release property upon dissolution (*i.e.*, substantially complete release of the drug within 30 minutes). See, paragraph [0081]. Because Kikuchi focuses on fast release, it teaches away from the sustained-release preparations of the present invention, and does not suggest that the present invention would have a reasonable expectation of success.

In sum, Kikuchi provides no teaching, suggestion or motivation to one skilled in the art for the sustained-release preparations of claim 1. Kikuchi does not suggest to one of ordinary skill in the art that the present invention would have a reasonable expectation of success. It has not been established that Kikuchi teaches or suggests each and every limitation of the instant claims. *See Motorola, Inc.*, 121 F.3d at 1473. Thus, instant claim 1 is not obvious by Kikuchi.

Claims 1-7 are Not Obvious over Kikuchi in View of Oshlack

Next, Claims 1-7 are rejected under 35 U.S.C 103(a) as being unpatentable over Kikuchi in view of Oshlack et al. (US 2002/0102302, “Oshlack”). (Pages 4-6 of the Office Action). It is alleged that Oshlack et al. teach a sustained release composition comprising tramadol (paragraph 0014), waxes (paragraph 0056), beeswax (paragraph 0056), hydrogenated vegetable oil (paragraph 0056), and additives (paragraph 0021), and therefore, it would have been obvious to a person of ordinary skill in the art to disclose a sustained release pharmaceutical preparation comprising tramadol and using two granulation processes, as taught by Kikuchi et al. in view of Oshlack et al. Office Action, pages 5-6. Applicant respectfully traverses the rejection.

As discussed above, Kikuchi fails to suggest or motivate the preparations obtained by the wet granulation using hydrophobic material as recited in claim 1. Oshlack does not cure the deficiency of Kikuchi.

Oshlack relates to a stabilized sustained release oral solid dosage form containing tramadol as an active agent. However, Oshlack, alone or in combination with Kikuchi, fails to disclose or suggest the preparations obtained by the wet granulation using hydrophobic

material as recited in claims 1-7. In Oshlack, the formulations are prepared via a melt extrusion/granulation technique. In Oshlack, the invention is to obtain formulations from which active ingredient can be released almost completely after curing process and release rate may be not changed during storage. Thus, Oshlack fails to teach or suggest essential elements of wet granulation using hydrophobic material in the claimed invention.

For example, paragraph [0004] of Oshlack discloses that the agents (e.g., waxes) used in sustained release dosage formulations often present problems of physical stability during storage because they undergo physical alterations on prolonged standing. To solve such problems, in Oshlack, the dosage form is cured at a suitable temperature, until an endpoint is reached at which the cured dosage form, when subjected to in-vitro dissolution, releases the tramadol in amounts which do not vary at any time point along the dissolution curve by more than about 20% of the total amount of tramadol released, when compared to the in-vitro dissolution of the formulation prior to curing. (paragraph [0018] and Claim 1). Therefore, Oshlack does not even teach or suggest any preparations obtained by the wet granulation using hydrophobic material of the present invention.

In view of the foregoing, neither Kikuchi nor Oshlack, alone or in combination, teaches or suggests the claimed sustained-release preparations. Nowhere does Kikuchi or Oshlack suggest or motivate to select the wet granulation using hydrophobic material. Thus, one of ordinary skill in the art would not have had a reasonable expectation of success from Kikuchi and Oshlack. A *prima facie* case of obviousness has not been established and the rejection must be withdrawn.

Obviousness-Type Double Patenting Rejection

Claims 1-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 11/572,326. (Office Action, pages 6-7).


Applicant requests that the rejection be held in abeyance until the claims of the present application are deemed otherwise allowable.

Conclusion

In view of the foregoing, all the rejections of the claims should be withdrawn. Reconsideration, entry of the above remarks, and allowance of the pending claims are respectfully requested. Should the Examiner not agree that all claims are allowable, a personal or telephonic interview is respectfully requested to discuss any remaining issues and to accelerate the allowance of the above-identified application.

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Respectfully submitted,



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